



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.: 09/508,913
Confirmation No.: 3738
Appellants : Stephen A. Udem et al.
Filed : March 16, 2000
For : Attenuated Respiratory Syncytial Viruses
Group Art Unit : 1648
Examiner : U. Winkler
Docket No. : 33,359
Customer No. : 25291

December 3, 2003

Mail Stop Appeal Brief - Patents
Hon. Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

APPELLANTS' REPLY BRIEF UNDER 37 C.F.R. 1.193(b)

Sir:

This Reply Brief is in response to the Examiner's
Answer mailed October 3, 2003. This Reply Brief is due
December 3, 2003. No fee is required for submission of this
Reply Brief.

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CERTIFICATION UNDER 37 C.F.R. 1.10

I hereby certify that this paper and the documents referred to as  
enclosed therein are being deposited with the United States Postal Service on  
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December 3, 2003

Date

Alan M. Gordon  
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This Reply Brief is submitted in triplicate.

Appellants will only discuss those points raised at pages 11-19 in the Examiner's Answer which are disputed or require correction by Appellants.

Argument

Claims 1 And 3 Are Fully Enabled By The Specification And Thus Do Comply With 35 U.S.C. 112, First Paragraph

The Examiner has rejected the Claims under 35 U.S.C. 112, first paragraph, as allegedly not enabled by the specification with respect to any single mutation in the polymerase region, even though the Examiner concedes the specification is enabling for the attenuated viral mutants that have multiple mutations (Paper No. 15, page 3).

In sum, the Examiner's rejection is premised on a concern that a person of ordinary skill in the art would have to engage in undue or extensive experimentation in order to ascertain whether a viral strain containing specific mutations would meet the limitation of the claims that the strain be attenuated.

The Examiner concedes that the Claims are enabled for an attenuated RSV that has multiple attenuating mutations. Further, the specification describes in detail

how the individual mutations are attenuating, as well as describing how to generate an RSV containing at least one attenuating mutation in the polymerase region, and how to test such a virus to ascertain whether it is sufficiently attenuated so as to lack pathogenicity while still being able to prevent disease (see discussion and citations at pages 18-20 of Appellants' Brief).

The factual situation here parallels that discussed in U.S. v. Teletronics Inc., 8 USPQ2d 1217, 1222, 1223 (Fed.Cir. 1988), where it was stated:

"A patent may be enabling even though some experimentation is necessary; the amount of experimentation, however, must not be unduly extensive.

\* \* \*

"Since one embodiment is admittedly disclosed in the specification, along with the general manner in which its current range was ascertained, we are convinced that other permutations of the invention could be practiced by those skilled in the art without undue experimentation. See SRI Int'l v. Matsushita Elec. Corp. of America, 775 F.2d 1107, 1121, 227 USPQ 577, 586 (Fed.Cir. 1985) (the law does not require an applicant to describe in his specification every conceivable embodiment of the invention); Hybritech Inc., 802 F.2d at 1384, 231 USPQ at 94 (the enablement requirement may be satisfied even though some experimentation is required)."

See also In re Strahilevitz, 212 USPQ 561 (CCPA 1982).

Appellants submit that, on balance, the factors listed in In re Wands, 8 USPQ2d 1400 (Fed.Cir. 1988), as

cited by the Examiner, are satisfied in the instant application, such that a skilled person would not have to engage in undue experimentation to practice the claimed invention. Appellants' specification describes in detail how to practice the claimed invention, whether the recombinant virus has one, two or the full array of mutations described and claimed (see discussion and citations at pages 18-20 of Appellants' Brief).

Therefore, in view of the foregoing facts and law, Appellants respectfully submit that the Claims satisfy 35 U.S.C. 112, first paragraph.

Claims 1 and 3 Are Not Anticipated By  
Randolph U.S. Under 35 U.S.C. 102(e)

The Examiner has rejected Claims 1 and 3 under 35 U.S.C. 102(e) as allegedly anticipated by Randolph U.S. In making this rejection, the Examiner has not taken into account the nature of the invention. In particular, the Examiner assumes facts not in the record regarding the total lack of accessibility of the nucleotide sequence of the RSV subgroup B wild-type strain with respect to the polymerase gene. That sequence takes up approximately forty percent

(40%) of the length of the total viral genome - over 6,000 base pairs.

The Examiner asserts at page 15 of the Examiner's

Answer:

"In response to 5) applicants argument that the wild type 2B strain was not deposited in U.S. Pat. No. 5,932,222 and therefore the key attenuating loci cannot be compared is not convincing. The claim is not drawn to a comparison of the isolated, attenuated human respiratory syncytial virus with the wild type virus, the wild type virus sequence referred to in the claim (SEQ ID NO:2) serves to allow for the alignment of the residues."

In response, Appellants first state that the comparison of the attenuated strains with the wild-type strain is a necessary predicate for the claims. Without such a comparison, one cannot identify which mutations are attenuating and cannot thereby generate recombinant attenuated strains containing all or less than all the attenuating mutations in the polymerase gene. The mutations recited in the claims are the result of these sequence comparisons.

Furthermore, the Examiner has incorporated into the prior art analysis the teaching of Appellants' application. This is clearly impermissible. The "wild type virus sequence referred to in the claim (SEQ ID NO:2)" is not disclosed in Randolph U.S. or in any other prior art

reference. The wild-type sequence was disclosed for the first time in Appellants' application.

The Examiner next makes the following unsupported statement (pages 15-16 of Examiner's Answer):

"As the deposited strains have originated from the wild type virus the numbering of the amino acid sequence would be conserved, indicating that 2B33F and 2B20L have the mutants at the indicated loci."

Appellants agree that the amino acid numbering may be conserved, but the sequences of the attenuated strains are most definitely not conserved. Having the sequences of the 2B33F and 2B20L mutant strains (supposedly through the depositing of those strains, which Appellants do not concede) in no way teaches or enables the sequence of the wild-type strain from which those mutant strains were derived. There is absolutely no scientific basis upon which the Examiner's assertion can be based.

Also important is the fact that Appellants' Claims recite that the attenuated RSV strains are recombinantly-generated. At the time Randolph U.S. was filed (1993), no techniques were available by which defined point mutations could be introduced into the genome of a non-segmented, negative-stranded RNA virus such as RSV. This made rational vaccine design impossible. Only with the discovery of the

rescue technology by Dr. Conzelmann in 1994 (cited as Bibliography entry 54 in Appellants' specification), did it become possible to insert desired attenuating mutations (identified by comparative sequence analysis) into the viral genome and to recover an isolated recombinant virus. A biologically or chemically derived virus strain, such as the 2B33F and 2B20L strains discussed by Randolph U.S., could not have been further modified, at the time Randolph U.S. was published, to specifically insert or delete other defined mutations, and thus fails to meet the claim limitation of "recombinantly-generated".

Therefore, because Appellants were the first to sequence the wild-type RSV strain (as well as vaccine strains), Appellants were able to be the first to identify the attenuating mutations in the RNA polymerase of RSV, which in turn are inserted into rationally designed recombinant viruses which are generated by rescue techniques which did not exist at the time Randolph U.S. was published.

For the reasons stated above, the claims are not anticipated by Randolph U.S.

Claims 1 and 3 Are Not Anticipated By  
Randolph EP Under 35 U.S.C. 102(b)

The Examiner has rejected Claims 1 and 3 under 35 U.S.C. 102(b) as allegedly anticipated by Randolph EP.

Randolph EP claims the same priority as Randolph U.S. and has essentially the same disclosure. Therefore, Randolph EP cannot anticipate the claims, for all the reasons set forth above with respect to Randolph U.S.

Claims 1 and 3 Are Not Subject To An Obviousness-Type  
Double Patenting Rejection Over Claims 7-10 Of Randolph U.S.

Finally, the Examiner has rejected Claims 1 and 3 as allegedly unpatentable under the judicially created doctrine of obviousness-type double patenting over Claims 7-10 of Randolph U.S.

In support of this rejection, the Examiner now relies on the Enzo case statement that "a reference in a patent specification to a deposit of genetic material may suffice to describe that material" (emphasis added).

It is significant that the Enzo opinion used the word "may" rather than "must". The issue is a fact-based inquiry. Here, Appellants are not claiming a raw sequence



per se of a viral strain. Instead, Appellants' claims are focused on the identification of attenuating mutations, where such mutations are based on a comparison of sequences of two biologically-derived strains with a wild-type strain which was not deposited by Appellants and was not sequenced in the prior art. Absent the availability of the sequence of the wild-type RSV strain, it was not possible for attenuating mutations to be identified in the deposited biologically-derived strains. Appellants' inventive contribution lies in the sequencing of the wild-type and biologically-derived mutant RSV strains, comparison of the sequences, identification of attenuating mutations in the polymerase gene, and the use of reverse genetics to recover recombinant viral strains which contain at least one of the attenuating mutations so identified. Randolph U.S. fails utterly to disclose or suggest such a concept, even taking into account the deposits of two mutant strains.

Therefore, for the reasons stated above, Appellants respectfully submit that pending Claims 1 and 3 are not properly subject to an obviousness-type double patenting rejection over Claims 7-10 of Randolph U.S., and this ground of rejection should be reversed.

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Conclusion

Appellants respectfully submit that, for the reasons discussed above, Claims 1 and 3 on appeal comply with 35 U.S.C. 112, first paragraph. Appellants further submit that Claims 1 and 3 on appeal are not anticipated by the prior art cited by the Examiner, nor are they subject to a double patent rejection. For the reasons set forth herein, Appellants respectfully urge that the Decision of the Examiner should be reversed and Claims 1 and 3 be allowed.

Respectfully submitted,



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